REMARKS

The foregoing amendments in the specification, claims and drawings correct minor inadvertent errors to make the application more clear and consistent.

Taking the amendments generally in page order, those on page 4 provide a spacing between words in lines 1 and 24.

On page 5, line 17, a second "," is omitted; at line 23, a misspelling is corrected.

On page 6, line 26, a misspelling is corrected.

On page 7, "2B" is changed to "2A" to reflect the proper relationship among the views.

On page 9, a proper antecedent basis is supplied to Fig. 27.

At pages 11, 20, 22, and 27, "then" is changed to --than-- to be grammatically correct.

On page 13, "Warner-Jenkins" is spelled correctly.

On page 15, the spelling of "degrees" is corrected, and a final "+" is omitted.

On page 16, the spelling of "diffraction" is corrected.

On page 18, a string of extraneous periods (".") are deleted. An extra period (".") is also deleted at page 19.

On pages 25 and 26, the spelling of "tablet" and "electroformed" are corrected.

On page 28, the plates 46 and 46' are correctly identified as such to correspond to the drawings.

On page 30, the rotating plate cooling position is identified as 121, not 120. 120 identifies the hub of the rotating assembly.

On page 33, the rails are correctly identified by number 178, as they are elsewhere in the specification and in the drawings.

In claim 2, hyphens are added to make it clear that the complete hyphenated phrases modify "coating".

In claims 9, 10, 14, 22 and 45, "claims" is changed to "claim" to be grammatically correct.

In claims 10 and 37, "pharmaceutical" and "holographic" are added to have a complete proper reference to the antecedent claims.

In claim 11, a redundant "in" is deleted.

In claim 18, a space is inserted between "1" and "which" in line 1.

In claim 19, "controllably" is correctly spelled, and the form of the multiple dependency is corrected.

In claim 22, "is" is inserted in line 2 for grammatical correctness.

In claim 23, "microrelief" is spelled correctly.

In claim 26, an extraneous "is" is deleted.

In claim 34, "wherever" is replaced by the standard "wherein" and "coat" is changed to "core", which is clearly what is intended.

The dependency of claim 36 on a later claim was clearly erroneous, and is now proper, claim 35.

The grammar of claim 38 is corrected by deleting "said" and inserting "is".

In claim 48, a "degree" temperature symbol is inserted after "150".

The amendments in Fig. 25 correct clear errors in the reference numbers so that they are consistent with the specification and avoid the use of the same number, "120", for two different items.

These amendments correct clear, minor errors. No new matter is introduced.

Entry of this Preliminary Amendment is respectfully requested.

Respectfully submitted,

Dated: August 20, 2002 By: Peter J. Manus

Peter J. Manus
Reg. No. 26,766
Dike Bronstein Roberts & Cushman
Intellectual Property Group of
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209
Tel: (617) 517-5530
Fax: (617) 439-4170

VERSION WITH ~~MARK~~INGS TO SHOW CHANGES MADE

In the Specification:

Paragraph beginning at line 15 of page 4 has been amended as follows:

Another object is to provide a visual quality control indication on each dosage form in the form of a hologram that visibly changes if the dosage form has been exposed to severe adverse conditions of temperature or humidity.

Paragraph beginning at line 24 of page 4 has been amended as follows:

Yet another object is to provide color and visual images and effects for food products and for pharmaceuticals, (1) without the use of FDA regulated colors, dyes, inks, or metals, or (2) with colors other than those which are FDA approved, or (3) with the use of FDA approved colorant only as a contrast color to make holographic effects and images more readily visible.

Paragraph beginning at line 17 of page 5 has been amended as follows:

a thermoformable solid outer layer overlaying said core, ~~,~~ and a microrelief in said layer.

Paragraph beginning at line 23 of page 5 has been amended as follows:

This layer is formed from an aqueous solution of a thermoformable material selected from the group consisting of modified cellulose, modified food starch, gelatin, waxes, vegetable gums, and combinations thereof. The preferred material comprises a modified cellulose, namely, ~~hydroxyproplymethlcellulose~~ hydroxypropylmethylcellulose (HPMC), hydroxypropylcellulose (HPC), and mixtures thereof.

Paragraph beginning at line 26 of page 6 has been amended as follows:

a conveyor that ~~carriers~~ carries the coated cores in a first direction,

Paragraph beginning at line 13 of page 7 has been amended as follows:

Fig. 2B is a view in side elevation of the tablet shown in Figs. 2 and ~~2B~~2A;

Paragraph beginning at line 15 of page 9 has been amended as follows:

Fig. 27 is a view in side elevation of the apparatus shown in Fig. ~~27~~26;

Paragraph beginning at line 15 of page 11 has been amended as follows:

One aspect of the present invention is the use of an outer layer 12 of a material that can receive a high resolution diffraction relief 16, and retain that relief pattern reliably for the intended life of the product, under anticipated conditions of manufacture, handling, storage and use. In particular, it has been found that certain materials can be: (1) formed into solid outer layers or coatings around a core, (2) subsequently heated to soften (including liquefy) the layers, (3) molded to form a high resolution diffraction relief, and then (4) cooled to retain that relief pattern in a solid form when (5) released or de-molded. General characteristics of these materials are that they have a controllable water-stability, are heat-formable, and are capable of being applied to the dosage form by known pan coating, printing, or laminating techniques. Such materials advantageously also produce coatings that are resistant to cracking, wrinkling, and/or crystallizing, can be made to flow or bond at a temperature lower ~~then~~ than that which will adversely effect the core, can retain a grating with a phase displacement on the scale of the wave length of light, are palatable, will not interfere with the release of the cores contents, and have controllable heat and water stability in storage so as to accurately control the fading or color. This controllable changes seen as a fading or color provides a readily visible indication of the environmental history of the dosage form, and its quality.

Paragraph beginning after the table on page 13 has been amended as follows:

The HPMC grades (e.g., "P5/6") above those of its manufacturer, Dow Chemical Co. "Spectraspray" is a trade description of a liquid colorant of ~~Warner-Jenkines~~Warner-Jenkins, Inc. "Marcoat" is a trade description of an aqueous shellac solution of Emerson, Inc. "DE 40" means "dextrose equivalency of 40%".

Paragraph beginning after the table on page 15 has been amended as follows:

In Examples 1 and 2 "Wt/ml" is the accumulated weight increase during the pancoating process in the dosage forms being coated, "ml" or "milliliter" being an approximate weight measure in grams given that one ml of water weighs one gram. Inlet and outlet Temp C are the air inlet and outlet temperatures to and from the coater in ~~dgrees~~degrees Centigrade. "CFM" is cubic feet per minute of this air flow through the coater and "Atm Air PSI" is the air pressure in coater in pounds per square inch. "RPM" is revolutions per minutes, the speed at which the drum of the coater rotates. "Spray g/min" is the rate in grams per minute that the aqueous solution of the material being coated is sprayed into the drum of the coater. "Time minute" is the elapsed during operation of the pancoating for that coating. ~~+~~

Paragraph beginning at line 8 after the table on page 16 has been amended as follows:

The coated tablets were stored for 3 weeks at 85° F and 65% relative humidity (RH). After the three week period, the tablets still retained an 80-90% ~~defraction~~diffraction efficiency. Tablets stored at similar temperatures, but at 80% RH, reached the point at which the microrelief started to fade, i.e., the point at which changes in the image on effect it produced became visible and/or detectable.

Paragraph beginning at line 7, page 18, has been amended as follows:

In the above preferred examples the outer coating 12 comprised two complete coatings, both being applied using conventional rotating drum "pan" coaters for tablets. Colorants in the first coating produce a desired background color for the dosage form and provide contrast for the holographic image or effect produced by the microrelief. It is also possible to add color to the core before compression~~.~~ Often the particle size of the aluminum lakes and titanium dioxide utilized in the first coating--if not fine enough--can interfere with the transfer process by sticking to the mold. This results in spotty, ineffective patterns. Thus, preferably, only the undercoat or the core carries a colorant; the overcoat is clear, and it is more stable.

Paragraph beginning at line 28, page 19, has been amended as follows:

Layers 12 formed of these materials are used to enclose the cores as in pan coating, or partially enclose a section of the core, as when they are applied using known printing or lamination techniques. If the layers themselves are formed into sections, the sections themselves can be used as dosage forms after being made to absorb therein the contents of the pharmaceutically active agent, as described below in more detail with reference to Fig. 10~~.~~.

Paragraph beginning at line 15, page 20, has been amended as follows:

A particular feature of a preferred embodiment of the invention is that the faces 18 as shown in Figs. 1-12 are characterized by 1) a shallow, convex curvature, generally along a circular arc as shown, or 2) a small flat recess. In general it is more difficult to transfer onto and then reconstruct a microrelief on a curved surface than a flat surface. Functionally, the degree of the curvature and the amount of the flat area at the outer surface of the dosage form should be such so as to resist the twinning of tablets during the coating process and allow for a good diffraction relief to be created (the pattern of ridges and grooves in the layer 12) and reconstructed (the viewed hologram). As a functional test of the appropriate degree of twinning, preferably twinning should be controlled to limit rejected twinned tablets to less than 0.5% of the total yield. As a functional test of the appropriate degree of pattern reconstruction, preferably diffraction efficiency should be not less ~~then~~than 80%. Increase of pan-coating rotation speed (RPM), spray rate (g/min), run time, as well as inlet and exhaust temperature and air pressure in the coater, all affect the amount of flat area and/or degree of shallowness of curvature that can be used before twinning affects limit yield. Preferred speeds rates and temperatures are described in the above examples.

Paragraph beginning at line 28, page 22, has been amended as follows:

Figs. 6 - 6C show yet another embodiment for a dosage form 10 in the form of a tablet with a core 14 coated with a layer 12 and having rounded shoulders 18b and a central recess 24 to control twinning, all according to the present invention. The Figs. 6 - 6C embodiments differ from the Fig. 5-5C embodiment principally in that the lettering 22 projects down rather ~~then~~than up in the central recess 26. Fig. 6C is a detailed sectional view taken along line C-C in Fig. 6 to illustrate the configuration of the recesses and the relative heights thereof. A microrelief 16 is typically formed in the layer 12 covering section 24. It may also be thermoformed in the surrounding bottom surface as well as the flat surface 18a surrounding both recesses 24 and 26. While the double recess dosage form configuration is more complex, it has the advantage of providing a flat surface 26 to receive a diffraction relief 16, while at the same time accenting the area around lettering 22. For purposes of illustration only, the dosage form shown in Figs. 6 - 6C, with the same general configuration and dimensions as the dosage forms shown in Figs. 4 and 5, has a maximum depth in the first recess 24 of approximately 0.0054 inch, and a the maximum depth of the second recess of approximately 0.0064 inch. As before the depth of the recess into which the microrelief is transferred also helps to protect it from abrasion. Again, these values are merely illustrative, and in no way should be construed as limiting the scope of this invention to that particular value, or even a near range of values.

Paragraph beginning at line 24, page 25, has been amended as follows:

Fig. 12C shows a ~~table~~ tablet 10 using a combination of the grooves 19 and 19'.

Paragraph beginning at line 20, page 26, has been amended as follows:

The transfer plate 32 is preferably formed as a thin, temperature resistant sheet of a material that can retain a high resolution microrelief such as a diffraction pattern on its outer surface, which is preferably thermally conductive and able to flex sufficiently to transfer the relief to a heat-softened and/or liquefied layer 12 on one face 18 (Figs. 1-12H) of dosage form 10 while accommodating to its shape. The preferred material is a diffractive surface composed of an ~~electoformed~~electroformed metal or a heat resistant plastic, both with a thickness in the range of 1 to 5 mils. The tension in the transfer plate 32 produces a downward pressure urging the microrelief pattern on the transfer plate to be replicated in the layer 12 on the dosage forms as they pass through a nip defined by the belt 34 (at the roll 36a) and the opposed portion of the transfer plate 32.

Paragraph beginning at line 3, page 28, has been amended as follows:

Figs. 16 and 17 show an alternative apparatus 45 according to the present invention which, like the apparatus 30 of Figs. 13-15, uses two transfer plates 46, 46' to replicate a high resolution diffraction relief on opposite faces 18 of dosage forms 10 carried in opening 48 of moving conveyor belt 50. The upper rim of belts 50 moves right to left, as shown, as dosage forms 10 are fed into the openings 48 which aligns and transports the dosage forms. The openings 48 extend through the belt 50. A panel 52 - - or a belt or other equivalent member - - supports the dosage forms at their bottom to retain them in the openings 48 before and after the

transfer plates ~~46, 4646~~, 46'. The transfer plates ~~46, 46~~ 46, 46' are each journalled on rolls 54a, 54b that drive the transfer plates in coordination with the movement of the belt 50. The transfer plates sandwich the dosage forms there between. Rolls 55 disposed behind each transfer plate adjacent the dosage forms are heated to heat the dosage forms through the transfer plates to a suitable temperature, again, preferably 90°C to 150°C. Cooling rollers 56 then help in demolding. Note that the thinness of the transfer plates not only facilitates rapid heat transfer, but also facilitates the application of a generally uniform pressure over the dosage form surface receiving the microrelief, despite the fact that the surface might not be flat, e.g., the curved surfaces 18 of the dosage forms 10 shown in Figs. 1-2. A uniform distribution of the pressure can be promoted by using a resilient pressure member, e.g., a foam sleeve on alternating rolls 54 and 54', and 56 and 56' below the dosage form such that each heating or cooling roller is pressing the bottom or top of the dosage form against an opposing resilient pressure member.

Paragraph beginning at line 22, page 30, has been amended as follows:

Fig. 25 shows a rotary apparatus 108 for thermoforming a high resolution diffraction relief onto a layer 12 on an array of dosage forms 10 carried in a pallet 71. A diffraction pattern transfer plate 76 is placed on each incoming pallet 71 at 110. The pallet is then transported to a position 112 where it is gripped between a pair of members 114, 116 each supported on the end of an arm 118 rotated by a hub 120. At least one arm 118 of each pair of pivots to open, close, and press the transfer plate towards the dosage forms. As the hub rotates, a gripped assembly is heated and pressed at angular position 119, cooled at position ~~120~~121, and released by opening the members 114, 116 at position 122 where the assembly is transported to a de-molding and transfer plate removal station 124.

Paragraph beginning at line 5, page 33, has been amended as follows:

The conveyor wheel 180 then rotates the dosage forms to a nip 184 where a heated cylinder 186 that carries a microrelief transfer plate 32' on its outer surface. A microrelief pattern, preferably a high resolution diffraction relief, is electroformed or otherwise created using known techniques on the outer surface of the plate 32' and positioned to contact the layers 12 on a first face of the dosage forms 10 as they pass through the nip 184. The heat of the cylinder 186 softens the layer 12 to replicate the microrelief pattern in it. The size of the nip spacing, in conjunction with particular dosage forms, transfer plates and carrier wheel constructions (e.g., with or without a resilient backing layer under the dosage forms like layer 77 in the Figs 21-24 embodiment) produces the desired degree of pressure to affect the replication for a given layer 12 and a given degree of heating. Also, with the foregoing embodiments, a pressure in the range of 5 to 15 kg/pill, and preferably about 10 kg/pill, is preferred. A guard rail (not shown) like rail ~~176~~178 may be used over the run to the nip 184, and in conjunction with other conveyor wheels runs, e.g.,to hold the dosage forms on the wheel 180 after they leave the nip 184 and continue to nip 188 where the dosage forms again transfer to conveyor wheel 190.

In the Claims:

Claim 2 has been amended as follows:

2. (Amended) A pharmaceutical dosage form according to claim 1 wherein said pharmaceutical dosage form further comprises a core comprising a pharmaceutically active substance and said layer is a solid all-covering or partially-covering coating overlying said core and said information is a holographic image or effect.

Claim 9 has been amended as follows:

9. (Amended) A pharmaceutical dosage form according to claims 8 wherein said outer layer completely covers said core.

Claim 10 has been amended as follows:

10. (Amended) A pharmaceutical dosage form according to claims 8, wherein said outer layer partially covers said core.

Claim 11 has been amended as follows:

11. (Amended) A pharmaceutical dosage form according to claim 7 wherein ~~in~~ said layer is formed from an aqueous solution of a thermoformable material selected from the group of modified cellulose, modified food starch, gelatin, waxes or vegetable gums and combinations thereof.

Claim 14 has been amended as follows:

14. (Amended) A pharmaceutical dosage form according to claims 8 or 9 wherein said outer layer is applied by printing or laminating.

Claim 18 has been amended as follows:

18. (Amended) A pharmaceutical dosage form according to claim 1 which consists essentially of said layer and, absorbed therein, a pharmaceutically active substance.

Claim 19 has been amended as follows:

19. (Amended) A pharmaceutical dosage form according to claims 9 ~~and~~ or 10 wherein said outer layer comprises at least one food grade material selected to ~~controllaby~~controllably display the effects of heat and/or humidity on said microrelief.

Claim 21 has been amended as follows:

21. (Amended) A pharmaceutical dosage form according to claim ~~18~~19 wherein said at least one food grade material retards the effects of heat on the holographic image or effect produced by said mircorelief a high melting point wax.

Claim 22 has been amended as follows:

22. (Amended) A pharmaceutical dosage form according to claims 8 or 9 wherein said solid outer layer is formed of food grade materials selected to controllably display the effects of moisture on the microrelief.

Claim 23 has been amended as follows:

23. (Amended) A pharmaceutical dosage form according to claim 22 wherein said at least one food grade material that responds to display the effects of moisture on the holographic image or effect produced by said ~~mircroreliefmicrorelief~~ is selected from the group consisting of a highly hygroscopic sugar ~~and~~ such as dextrose or a plasticizer such as propylene glycol.

Claim 26 has been amended as follows:

26. (Amended) A pharmaceutical dosage form according to claim 25 in which the modification ~~is~~ comprises a reduction in the amount of flat areas on the core.

Claim 27 has been amended as follows:

27. (Amended) A pharmaceutical dosage form according to claim 26 in which the modification comrpises said core having at least one convexly curved face of not less ~~then~~than .6 radians.

Claim 34 has been amended as follows:

34. (Amended) The holographic dosage form production method of claim 30 ~~wherever~~wherein said twinning control comprises forming said core with a recess within at least one face of said ~~coat~~core, said recess having a generally flat bottom that receives said coating layer.

Claim 36 has been amended as follows:

36. (Amended) The holographic dosage form production method of claim ~~42~~35 wherein said recess is less than about 0.01 mm.

Claim 37 has been amended as follows:

37. (Amended) The ~~diffractive~~holographic dosage form production method of claim 29 wherein said coating includes said thermo-formable material bonding reliably with said core.

Claim 38 has been amended as follows:

38. (Amended) The holographic dosage form production method of claim 29 or 37 wherein ~~said~~ thermo-formable material is selected from the group consisting of: gelatin, hydroxypropylmethylcellulose (HPMC), hydroxyproplycellulose (HPC), modified food starches, waxes, vegetable gums and combinations thereof.

Claim 45 has been amended as follows:

45. (Amended) The holographic dosage form production method of claims 41 or 43 wherein said coated core facing said plate during said pressing is non-planar, and said belt flexibility is sufficient to allow said belt to conform to said non-planar coating desiring said pressing.

Claim 48 has been amended as follows:

48. (Amended) The holographic dosage form production method of claim 47 wherein said heating raises the temperature of said diffraction pattern on said belt to a temperature in the range of ~~90-150 C.~~90-150°C.

Claim 53 has been amended as follows;

53. (Amended) Apparatus for the continuous production of a hologram on an ingestible dosage form having a core which can contain a pharmaceutically active substance and which has been coated with a thin layer of a thermo-formable, comprising,

a conveyor that ~~carriers~~carries the coated cores in a first direction,

a plate containing a holographic diffraction pattern on one surface thereof facing the coated cores on said conveyor, said plate being movable along said first direction in coordination with said carrying of said conveyor and with said one surface spaced from said coated cores,

a heater for rapidly raising the temperature of one of said plate and said coating to a level where said coating is formable, apparatus for pressing said one surface into said coating after said heating to replicate said diffraction pattern on said coating,

a cooler to rapidly lower the temperature of said coating to stabilize said diffraction pattern in said coating, and

apparatus to separate said one surface from said coating.